

## Appendix A

### VERSION WITH MARKINGS TO SHOW CHANGES MADE

41. (Amended) A recombinant yeast cell comprising:

a heterologous G protein coupled receptor that, upon ligand stimulation,  
activates an endogenous yeast pheromone response pathway,

wherein an endogenous yeast gene encoding a [protein] phosphatase that negatively regulates the yeast pheromone system pathway is mutated to render the protein nonfunctional such that signals generated by ligand binding to the receptor are amplified.

43. (Amended) The yeast cell of claim 41 [42], wherein the endogenous gene encoding the phosphatase is selected from the group consisting of: MSG5, PTP2, and PTP3.

46. An assay to identify compounds that modulate the activity of a receptor, comprising:

- (i) providing a recombinant cell as claimed in claim 1, 8, 32, or 41 [or 44], wherein a detectable signal is produced in the cell upon stimulation of the receptor;
- (ii) contacting the cell with a test compound; and
- (iii) identifying a compound which induces a change in the detectable signal in the cell, such a change indicating that the compound modulates the activity of the receptor.

51. (New) A recombinant yeast cell comprising:

(i) a heterologous G-protein coupled receptor that, upon ligand stimulation, activates the endogenous yeast pheromone response pathway; and

(ii) a heterologous DNA construct comprising a gene encoding STE5, which STE5 activates the yeast pheromone response pathway, which gene is operably linked to a promoter

that is responsive to activation of the yeast pheromone response pathway, wherein stimulation of the receptor by a ligand leads to expression of the gene encoding STE5 that activates the yeast pheromone response pathway such that signals generated by ligand binding to the receptor are amplified.

52. (New) A recombinant yeast cell comprising:

(i) a heterologous G-protein coupled receptor that, upon ligand stimulation, activates the endogenous yeast pheromone response pathway; and

(ii) a heterologous DNA construct comprising a gene encoding a protein that activates the yeast pheromone response pathway, which gene is operably linked to a promoter that is responsive to activation of the yeast pheromone response pathway, wherein stimulation of the receptor by a ligand leads to expression of the gene encoding the protein that activates the yeast pheromone response pathway such that signals generated by ligand binding to the receptor are amplified, wherein said gene is selected from the group consisting of STE4, STE5, STE11, STE12, STE20 and FUS3.